# A COMPARISON OF THE WASSERMANN AND NOGUCHI COMPLEMENT FIXATION TESTS

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# A COMPARISON OF THE WASSERMANN AND NOGUCHI COMPLEMENT FIXATION TESTS *

By Howard Fox, M. D., New York.

BEFORE analyzing the practical results obtained by a comparison of the Wassermann[1] and Noguchi[2] tests it seems advisable to discuss the advantages and disadvantages of the methods from a theoretical standpoint. At the outset it may be said that the present communication is solely concerned with the complement-fixation test recently described by Noguchi and not with the serum diagnosis test of the same author depending upon the precipitation of globulin by butyric acid.[3]

Up to the present time four methods for the serum diagnosis of syphilis, depending upon the principle of complement-fixation have been devised, which may be said to be independent "systems." In addition there are three other methods also depending on the same principle (complement-fixation), which are merely attempts at simplification of the original Wassermann test.

The first two systems to be published were those of Wassermann and of Detre,[4] that of Detre appearing only two weeks after the now classic communication of Wassermann, Neisser and Bruck. As the publication of the two methods was practically simultaneous and entirely independent, it seems unjust that at least some share of credit should not have fallen to Detre. The latter's method seems to be at least theoretically the equal of Wassermann's.

The chief weakness in the method of Wassermann is due to the fact that there is amboceptor for sheep's corpuscles naturally present in human blood. This may be present in such excess (as Noguchi has shown) as to give a negative reaction where a positive one should be given. An analogous objection can be made to the method of Detre in which horse's corpuscles and anti-horse amboceptor are used. It has been found by Aschenheim[5] that there is normally present in human blood a certain amount of amboceptor for horse's corpuscles. A further objection of minor importance to

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Detre's method is that rabbit's serum, which he uses for complement, is somewhat less sensitive to fixation than guinea pig serum.

Of the three modifications of the regular Wassermann reaction, that of Bauer[6] has received the greatest amount of attention. This method dispenses with the immune anti-sheep amboceptor and depends alone upon the anti-sheep amboceptor that is naturally present in human blood. As this is a variable quantity and at times insufficient in amount to cause complete hæmolysis, the method is on this account objectionable.

The modifications of Hecht[7] and of Stern[8] utilize the complement normally present in fresh human serum. Against the methods such as these which use human, instead of guinea pig complement, the following objections can be made: Human complement is less sensitive to fixation and more variable in amount than guinea pig complement and its use requires that the test be made with a fresh specimen of blood, as complement rapidly deteriorates. Again there is no direct way of testing the anti-complementary action of the antigen, when human complement is used, that is, it cannot be directly told whether the inhibition of hæmolysis is due to the antigen alone or to the antigen combined with the antibody. Finally as there is no complement in the spinal fluid this substance cannot be used for the methods depending upon the presence of human complement. The modification of Hecht uses not only human complement, but natural amboceptor as well. It is, therefore, not only open to the objections urged against the use of human complement, but also to the objections to natural amboceptor discussed above in connection with Bauer's modification.

Recently two systems have been devised independently by Tschernogubow[9] and by Noguchi, both of which employ human corpuscles and anti-human amboceptor. In his effort to obtain the greatest possible simplicity, Tschernogubow used a single drop of blood which was depended upon to supply corpuscles, antibody and complement. The test is open to the objections mentioned above for using human complement. Furthermore, the amount of complement present in a drop of blood is too small according to the experiments of Noguchi[10] to hæmolyse a weak suspension of human corpuscles in the presence of two units of amboceptor. Tschernogubow's method cannot be used for testing old specimens, not merely because he uses human complement (which deteriorates rapidly), but also because the human corpuscles deteriorate after a few days.

That the method of Tschernogubow is as faulty in practice as it is objectionable in theory would appear from a recent communication of the author of the test. He practically repudiates his method by proceeding to describe an entirely new one which he calls merely a "change" in his old method. Tschernogubow[11] in his new test uses guinea pig corpuscles as the indicator and apparently uses human complement and natural anti-guinea pig amboceptor though this is not stated. While it is quite possible that this second method will work out in practice it is certainly not a very great step forward and by no means free from theoretical objections.

The two principal objections to the above described methods, namely the presence of natural anti-sheep amboceptor in human blood, and the substitution of human for guinea pig complement do not apply to the recently perfected system of Noguchi. A possible theoretical objection to Noguchi's method might be made, that as the serum is used in an active state the test is thereby rendered too delicate and too liable to give positive reactions where negative ones should be given. Boas,[12] in a recent communication, has compared the effects of using active and inactive serum in non-syphilitic affections. His results show that by using active serum more positive reactions were obtained in non-syphilitic cases than had previously been supposed to be possible. Boas concludes that it is not practicable to use active serum. He considers that it is necessary by means of inactivation, to weaken the syphilitic antibodies, in order to effect a narrower zone of reaction. It is also necessary to destroy natural complement which in some cases is present in large amount. The objection of using active serum cannot be held against the system of Noguchi as in his method it is possible to use either serum that is active (fresh), or inactive (without complement) or inactivated (heated to 56° C.). This cannot be said of any of the other systems described. If, however, inactivated serum is used in the Noguchi test it is necessary according to Noguchi (personal communication) to employ four to five times the usual amount of serum, *e. g.*, four or five capillary drops instead of one. With regard to the disturbing influence of human complement in the Noguchi test it may be said that the amount of complement (human) in one capillary drop of serum is so small that its effect can be disregarded. The question of using active serum in the Noguchi test can, after all, only be decided by the practical results of the test, a subject which will be later discussed.

The technique employed by the writer in his comparative analy-

sis was practically that originally recommended by Wassermann and by Noguchi for their respective methods. In the case of the Wassermann test several substances were used as antigen. For some of the earlier tests a 0.1 per cent. suspension of crude lecithin (as prepared and titrated by Noguchi) was used. For a few tests an extract of dog liver kindly supplied by Dr. H. F. Swift served as an excellent antigen. In the majority of the cases, extracts of liver of syphilitic infants were used, their preparation being as follows: To the liver substance previously ground in a mortar, alcohol was added in the proportion of one part of liver substance to ten of alcohol. The mixture was allowed to stand ten days at room temperature, being shaken from time to time. The clear fluid was then evaporated to one-third its volume and used for the test in dilution with normal salt solution in the proportion of four parts of salt solution to one of extract. The other substances used were two cubic centimeters of inactivated patient's serum, one-tenth cubic centimeter of guinea pig complement, two units of anti-sheep amboceptor, prepared from rabbits and one cubic centimeter of a five per cent. suspension of washed sheep's corpuscles, the entire mixture consisting finally of five cubic centimeters of fluid. The tubes were incubated in a water bath at 37° Centigrade and the results read at the end of two hours.

The technique of the Noguchi test was that originally described by Noguchi and by the writer[13] in a former communication. For complement 0.04 cubic centimeter of fresh guinea pig serum was employed instead of the papers impregnated with this substance. The suspension of corpuscles was made by mixing one drop of normal blood in four cubic centimeters of normal salt solution, while the antigen and amboceptor were used in the form of small papers kindly supplied by Dr. Noguchi. The tubes were incubated for two hours, after which the final results were read.

As the suspension of corpuscles shows at times anti-hæmolytic properties, Dr. Noguchi has recently advised that the corpuscles be washed free of the disturbing anti-hæmolytic substances. This is most conveniently done by allowing the corpuscles to settle to the bottom of the flask, after which the salt solution is pipetted or poured off and fresh salt solution added.

In an attempt to judge of the merits of the Wassermann and Noguchi tests from a practical standpoint, the writer has made a comparison of the two methods in 210 cases. Of this number twenty-three were non-syphilitic control cases, while the remainder were

TABLE I

CASES OF SYPHILIS WITH MANIFEST LESIONS.

| *Case No.* | ** Stage* | *Type* | *Time since infection* | *Treatment* | *Wassermann* | *Noguchi* |
|---|---|---|---|---|---|---|
| 1 | II | Papular | 4 months | 3 weeks internal | + | + |
| 2 | II | Papular | Probably 1 year | 3 weeks internal | + | + |
| 3 | III | Gummatous | Probably 5 years | 4 months internal | −+ | + |
| 4 | III | Leucoplakia | 15 years | 6 weeks inunctions, 1 year internal | − | + |
| 5 | III | Tubercular | Probably 15 years | 1 month internal | − | + |
| 6 | II | Macular | Few months | None | − | + |
| 7 | III | Gummatous | 7½ years | 2 years inunctions and internal | + | + |
| 8 | II | Papular | 4 months | None | ++ | ++ |
| 9 | II | Papulo-squamous | 3 months | 2 months internal | −+ | ++ |
| 10 | III | Tuberculo-gummatous | Unknown | 4 months internal | ++ | ++ |
| 11 | III | Gummatous | 23 years | 20 months internal | + | + |
| 12 | III | Gummatous | Unknown | None | − | + |
| 13 | II | Papular | 3 months | None | ++ | ++ |
| 14 | III | Gummatous | 4 years | 1 year internal | + | + |
| 15 | II | Maculo-papular | Few months | None | ++ | ++ |
| 16 | II | Maculo-papular | 1 month | 2 weeks internal | ++ | ++ |
| 17 | III | Tubercnlo-ulcerative | 3 years | 9 months | + | + |
| 18 | II | Macular | 2 months | None | ++ | ++ |
| 19 | III | Ulcerative and gummatous | Unknown | 4 years internal | −+ | ++ |
| | | | | Most of time under internal treatment | −+ | − |
| 20 | III | Leucoplakia | 9 years | None | | |
| 21 | II | Papulo-squamous | Unknown | None | ++ | ++ |
| 22 | III | Gummatous | Unknown | 10 days medicine | −+ | + |
| 23 | III | Tubercular | 7 years | 90 injections | − | −+ |
| 24 | III | Tubercular | 6 years | "Always under treatment," internal | −+ | + |
| 25 | II | Papulo-pustular | 7 months | None | ++ | + |
| 26 | III | Tuberculo-ulcerative | Unknown | None | − | −+ |
| 27 | II | Macular | 6 weeks | None | + | + |
| 28 | II | General adenitis | 9 weeks | 5 injections | ++ | ++ |
| 29 | III | Gummatous | 14 years | Large amount internal | −+ | − |
| 30 | II | Papulo-squamous | 4 months | 3 months internal | + | ++ |
| 31 | III | Tuberculo-squamous | Unknown | None | −+ | + |
| 32 | II | Macular | 9 weeks | 1 week internal | ++ | ++ |
| 33 | II | Macular | 2½ months | 1 week internal | ++ | ++ |
| 34 | II | Mucous patches | 3 months | 2 months internal | ++ | + |
| 35 | II | Papular | 5 weeks | 10 days internal | ++ | ++ |
| 36 | I | Chancre | 11 days | None | + | + |
| 37 | II | Papular-corymbyform | 1 year | 4 months internal | + | + |
| 38 | II | Papular | 2 months | 2 weeks internal | ++ | ++ |

| Case No. | * Stage | Type | Time since infection | Treatment | Wassermann | Noguchi |
|---|---|---|---|---|---|---|
| 39 | II | Papular | 3½ months | None | ++ | ++ |
| 40 | III | Tubercular | 6 years | 1½ years internal | −+ | + |
| 41 | II | General adenopathy (recent roseola) | 2 months | None | ++ | ++ |
| 42 | II | Mucous patches | 3½ months | 27 injections | + | + |
| 43 | III | Leucoplakia | 3 years | None | −+ | + |
| 44 | III | Tubercular | Unknown | None | −+ | −+ |
| 45 | — | Hereditary | ——— | None | −+ | −+ |
| 46 | III | Tubercular | 18 years | 2 months internal | + | + |
| 47 | II | Macular | 3 months | None | + | + |
| 48 | II | Papular | 9 months | 20 injections | + | + |
| 49 | III | Choroiditis | 8 years | Large amount of injections and inunctions | − | − |
| 50 | II | Maculo-papular | 2 months | None | ++ | ++ |
| 51 | III | Tubercular | Unknown | 3 years internal | ++ | ++ |
| 52 | I | Chancre of lip | | None | + | −+ |
| 53 | II | Macular | 6 months | Internal since beginning | + | + |
| 54 | II | General adenopathy | 3 months | 8 injections | ++ | ++ |
| 55 | III | Tubercular | 6 years | 3 years internal | + | + |
| 56 | II | Maculo-papular | Few months | None | + | ++ |
| 57 | III | Tubercular | Unknown | None | + | ++ |
| 58 | II | Macular | Few months | None | ++ | ++ |
| 59 | III | Tubercular | 6 years | 1½ years internal | + | ++ |
| 60 | II | Papular | Few months | None | ++ | ++ |
| 61 | II | Pustulo-crustaceous | Unknown | None | ++ | ++ |
| 62 | III | Tubercular | 17 years | 3 years internal | + | + |
| 63 | III | Tubercular | Unknown | None | − | − |
| 64 | III | Tubercular | 3 years | 2½ years | − | −+ |
| 65 | III | Tubercular | Probably 6 years | 6 months, injections and internal | ++ | ++ |
| 66 | II | Macular | 2 months | None | ++ | ++ |
| 67 | I | Chancre | 1 month | None | + | + |
| 68 | II | Pustular | 5 months | None | ++ | −+ |
| 69 | I | Chancre | 1 month | None | + | + |
| 70 | III | Tubercular | 13 years | 2 months internal | ++ | ++ |
| 71 | I | Chancre tonsil | 2 months | None | ++ | ++ |
| 72 | III | Leucoplakia | 35 years | 7 months internal | − | − |
| 73 | II | Macular | Recent | None | + | + |
| 74 | II | Macular | 3 months | None | ++ | ++ |
| 75 | I | Chancre of penis | 1 month | None | + | ++ |
| 76 | I | Chancre of penis | 2 months | None | + | + |
| 77 | II | Papulo-squamous | 2½ months | None | + | + |

*I—Primary.
II—Secondary.
III—Tertiary.

TABLE II

CASES OF SYPHILIS SHOWING NO MANIFESTATIONS.

| *Case No.* | *Time since infection* | *Treatment* | *Wassermann* | *Noguchi* |
|---|---|---|---|---|
| 1 | Unknown | 1 year internal | — | —+ |
| 2 | Probably 18 months | 4 months internal | — | —+ |
| 3 | 18 months | 1 year | ++ | ++ |
| 4 | 10 years | 2 years internal | — | + |
| 5 | 2 to 4 years | 10 injections and internal for 2 years | — | — |
| 6 | 6 months | 5 months internal | ++ | ++ |
| 7 | 9 years | About 3 years internal | —+ | —+ |
| 8 | 16 years | 6 years internal. Injections at present | — | —+ |
| 9 | 3 years | 3 years internal | — | + |
| 10 | Probably 2½ years | 2 years internal | — | —+ |
| 11 | Probably 2½ years | 2 years internal | — | — |
| 12 | 9 weeks | 2 weeks internal | ++ | ++ |
| 13 | 4 years | 3 years | + | + |
| 14 | 12 years | 3 years internal and injections | — | ++ |
| 15 | 10 years | Large amount internal | — | + |
| 16 | 18 years | 6 months internal | — | — |
| 17 | 2 years | 2 years | — | — |
| 18 | 4½ years | 4 years internal, 4 months injections | — | — |
| 19 | 20 months | 20 months internal | — | — |
| 20 | 4 months | 12 injections | + | + |
| 21 | 2 years | 2 years internal | + | + |
| 22 | 1 year | 1 year internal | — | — |
| 23 | 15 years | About 6 months internal | —+ | — |
| 24 | 14 months | 14 months internal | —+ | + |
| 25 | 15 months | 6 weeks internal and inunctions | —+ | + |
| 26 | 10 years | About 1 year internal | — | —+ |
| 27 | 9 years | 2 years internal | — | — |
| 28 | Unknown | | + | + |
| 29 | 6 years | 2½ years internal. Occasional inunctions | — | —+ |
| 30 | 25 years | None | — | — |
| 31 | 9 months | 50 inunctions, 15 injections | —+ | + |
| 32 | 3½ years | 3½ years internal | + | + |
| 33 | Probably 1½ years | 1 year internal | ++ | ++ |
| 34 | Unknown | | + | + |
| 35 | 4 years | 4 years inunctions and injections | + | —+ |
| 36 | 13 years | About 4 years internal. Few inunctions | — | + |
| 37 | 20 years | 2 years internal | — | — |
| 38 | 3½ years | Irregular 3 years internal | + | —+ |
| 39 | 2 years | 2 years injections | + | + |
| 40 | 10 years | 6 months internal | — | — |
| 41 | 2 years | 2 years internal | ++ | ++ |
| 42 | 3 years | 1 year injection, 2 years internal | —+ | + |
| 43 | 8 years | 3 series of inunctions | —+ | + |
| 44 | 8 years | 3 years internal | —+ | — |
| 45 | 5 years | 9 months internal | — | — |

| Case No. | Time since infection | Treatment | Wassermann | Noguchi |
|---|---|---|---|---|
| 46 | 2⅓ years | 2⅓ years internal | — | — |
| 47 | 3 years | 3 years internal | + | + |
| 48 | 10 years | None | + | + |
| 49 | 2½ years | 18 months internal | — | — |
| 50 | 10 years | 3 years internal | — | — |
| 51 | 15 years | 4 years inunctions and internal | — | — |
| 52 | 18 years | 18 months internal | —+ | —+ |
| 53 | 4 years | 200 injections | — | — |
| 54 | 14 years | Large amount of inunctions and injections | — | — |

## TABLE III
## CASES FOR DIAGNOSIS.

| Case No. | Disease | Wassermann | Noguchi | Remarks |
|---|---|---|---|---|
| 1 | Scabies—possible recent syhilis | ++ | ++ | Case could not be followed. |
| 2 | Traumatic vs. syphilitic ulcer of lip | — | — | No history of syphilis. Patient has bad teeth. |
| 3 | Chancre vs. chancroid | — | — | Butyric acid test negative. |
| 4 | Drug rash vs. macular syphilide | ++ | ++ | Proved later to be syphilitic. |
| 5 | Lateral sclerosis. Gummata? | — | —+ | Improved under potassium iodide. |
| 6 | Scabies vs. syphilis | — | — | Proved to be non-syphilitic. |
| 7 | Epithelioma vs. syphilis of glans penis | — | — | Proved to be epithelioma under microscope |
| 8 | Endarteritis with symptoms of Raynaud's disease | — | — | Case well treated. |
| 9 | Gumma of tonsil | + | + | Great improvement under potassium iodide. |
| 10 | History of miscarriages | — | — | |
| 11 | Epithelioma vs. syphilis of tongue | —+ | —+ | Probably epithelioma. |
| 12 | Chancre vs. chancroid | + | + | |
| 13 | Lupus erythematosus vs. syphilis | + | ++ | Probably both diseases present. |
| 14 | Syphilophobia | — | — | |
| 15 | Rhinitis syphilitica? | — | — | History indefinite. |
| 16 | Fibromata vs. gummata | — | ++ | Cured by anti-syphilitic treatment. |
| 17 | History of recent condylomata | ++ | + | |

| Case No. | Disease | Wassermann | Noguchi | Remarks |
|---|---|---|---|---|
| 18 | Chancre (?) of clitoris | — | — | Proved to be non-syphilitic. |
| 19 | Seborrhœic dermatitis vs. tubercular syphilide | + | + | Cured by anti-syphilitic treatment. |
| 20 | Eczema vs. syphilis of palm | — | — | Proved to be eczema. |
| 21 | Tuberculous vs. syphilitic ulceration of palate | ++ | ++ | Improving under anti-syphilitic treatment. |
| 22 | History of miscarriages | — | — | |
| 23 | Possible syphilis of tubes and ovaries | + | + | |
| 24 | Scrofuloderma vs. hereditary syphilis | ++ | ++ | Rapid cure under anti-syphilitic treatment. |
| 25 | Eczematous vs. syphilitic ulcer of leg | —+ | + | Case not followed. |
| 26 | Rosacea vs. tubercular syphilide of nose | —+ | —+ | Positive history syphilis. Improvement only under treatment for rosacea. |
| 27 | Leucoplakia—possible previous syphilis | — | — | |
| 28 | Ulceration of tonsil | — | + | |
| 29 | Syphilophobia | — | — | |
| 30 | Gonorrhœa plus suspected chancre | ++ | ++ | Later proved to be syphilis. |
| 31 | Onychia | — | — | No history of syphilis. |
| 32 | Tuberculous vs. syphilitic ulceration of throat | + | + | |
| 33 | Dactylitis? | — | — | Probably a synovitis of nervous origin. |
| 34 | Ulceration of throat | —+ | —+ | |
| 35 | Recent suspicious sore of penis | — | — | No symptoms of syphilis. |
| 36 | Rosacea vs. tubercular syphilide | — | —+ | Case not followed. |
| 37 | Lupus erythematosus vs. tubercular syphilide | — | — | Proved to be lupus. |
| 38 | Syphilophobia | — | — | |
| 39 | Fibromata vs. gummata | — | — | No history of syphilis. |
| 40 | Tuberculide vs. syphilide | — | — | No history of syphilis. |
| 41 | Atrophy of nails. Hereditary syphilis? | — | — | |
| 42 | Eczema. Hereditary syphilis? | —+ | + | Sister of case 4. Daughter of case 48 (Table I.) |
| 43 | Inguinal adenitis. Ulceration of throat | — | — | Later proved to be non-syphilitic. |
| 44 | Ulceration of epiglottis | + | + | Possible chancre 15 years previously. |

| Case No. | Disease | Wassermann | Noguchi | Remarks |
|---|---|---|---|---|
| 45 | Chancre vs. chancroid | — | — | Proved to be non-syphilitic. |
| 46 | Urethral chancre? | — | + | Later both tests gave strong positive reactions. |
| 47 | Carcinoma vs. tuberculosis vs. syphilis of rectum | — | — | Syphilis later exeluded. |
| 48 | History recent sore of penis | — | — | No further signs of syphilis. |
| 49 | History reeent sore of penis | — | — | No further signs of syphilis. |
| 50 | Induration of glans penis | —+ | —+ | |
| 51 | Phagedænic ulcer vs. gumma of glans penis | —+ | —+ | Too recent for further report. |
| 52 | Retrobulbar neuritis. Possible tabes | -- | — | Doubtful history of syphilis. Tabes exeluded later. |
| 53 | Syphilophobia | — | — | |

TABLE IV

SUMMARY OF STATISTICS.

| Disease | Total Number of Cases | Wassermann tests Positive reactions | Wassermann tests Percentage | Noguchi tests Positive reactions | Noguchi tests Percentage |
|---|---|---|---|---|---|
| Primary | 7 | 7 | 100% | 7 | 100% |
| Secondary | 37 | 36 | 97% | 37 | 100% |
| Tertiary | 32 | 23 | 71% | 27 | 84% |
| Hereditary | 1 | 1 | — | 1 | — |
| Tabes dorsalis | 3 | 3 | 100% | 3 | 100% |
| Latent cases | 54 | 25 | 46% | 34 | 62% |
| Cases for diagnosis | 53 | 21 | 39% | 26 | 49% |
| Non-syphilitic eases | 23 | 2 | — | 4 | — |

cases of manifest and latent syphilis in its different stages and cases in which the diagnosis was in doubt.

A detailed comparison of the results of the two methods in individual cases is given in Tables 1, 2 and 3. A positive reaction is represented by a single plus sign, while two plus signs signify a strong reaction or practically complete inhibition of hæmolysis. A weak positive reaction is represented by minus plus and a negative by a minus sign. From these tables and from the summary in Table 4, it will be seen that a higher percentage of positive reactions is given by the Noguchi than by the Wassermann tests. It may, however, be said that as the writer's experience has increased, the

number of positive reactions obtained from the regular Wassermann tests have increased and at present the results from the two methods are more nearly parallel than at first.

Of the 77 cases (Table I) with manifest lesions of syphilis, 67 or 87% gave positive reactions with the Wassermann and 72 or 93% gave positive reactions with the Noguchi test. Of the 77 cases, 37 belonged to the early period, most of them to the first few months of the disease. All of these were positive with the Noguchi and all except one were positive with the Wassermann test. In this case, one of septic metritis and syphilis combined, it was impossible to obtain a second specimen of blood for examination. Of the 32 cases classed as tertiary 23 or 71% gave positive Wassermann and 27 or 84% positive Noguchi reactions.

Seven cases of primary syphilis were examined in which the diagnosis was fairly positive from a clinical standpoint. In one case (a chancre of the lip), the lesion had existed only eleven days. In most of the cases, however, the lesions were of several weeks' duration. One patient presented a well marked lesion of the tonsil that had existed two months and that showed very typical glandular enlargement. All of these cases gave positive reactions, in four cases the diagnosis being confirmed by positive spirochæta findings with the dark field illuminator. In addition nine patients were examined in which the diagnosis of chancre was doubtful. Of these cases four gave a positive reaction and five a negative reaction with both tests. Of the four cases which gave a positive reaction, three proved later to be undoubtedly syphilitic. The fourth case was not able to be followed. The five cases which gave a negative reaction remained untreated, and did not present later any manifestations of syphilis.

That the Wassermann reaction can at times compete with the examination for spirochætæ, is well illustrated by one of the doubtful cases of chancre which gave a positive reaction. In this case the patient had suffered from gonorrhœa for about three weeks when a suspicious induration was felt beneath a very tight foreskin. The lymphatic vessels of the penis were enlarged and hard and there was a moderate inguinal adenitis of specific type. The examination for spirochætæ was practically impossible owing to the phimosis, and the Wassermann test which was made cleared up the diagnosis by giving a very strong positive reaction.

Of the 54 cases of syphilis showing no manifestations (Table

II), 25 or 46% gave positive reactions with the Wassermann test and 34 or 62% positive reactions with the Noguchi test.

Of the 53 cases for diagnosis (Table III), 21 or 39% gave positive Wassermann and 26 or 49% positive Noguchi reactions. In the majority of these doubtful cases the results were conclusive and in some cases of considerable interest. It may be of interest to cite the case of a child from the Skin and Cancer Hospital in which the diagnosis lay between an extensive scrofuloderma and hereditary syphilis. The case was seen by a dozen or more of the assistants, half of them firmly holding to one and half to the other diagnosis. The test gave a very strong positive reaction and the diagnosis of syphilis was confirmed by the rapid disappearance of the lesions under inunctions of blue ointment. Owing to an error in diagnosis, the child before admission to the hospital, had worn a plaster jacket four years for a supposed tubercular affection which did not exist.

The limitations of the Wassermann reaction, in that a positive test merely indicates the presence of syphilis and does not prove that a certain lesion is syphilitic, are well illustrated by the following case. The diagnosis in this case lay between lupus erythematosus and syphilis, with the clinical evidence strongly in favor of the former affection. As a positive reaction was obtained the patient was put upon antisyphilitic treatment. The failure, however, of treatment and the results of a biopsy showed the lesion to be conclusively lupus erythematosus. Upon questioning the patient closely, a history of a number of miscarriages was obtained, making it probable that at the time of examination she was suffering from both lupus erythematosus and syphilis. Space will not allow a further discussion of the doubtful cases, some of which have already been described in a previous communication of the writer's.

Of the twenty-three non-syphilitic cases examined, two gave weak positive reactions with the Wassermann and Noguchi tests. These were cases of leprosy which according to the reports of Meier,[14] Jundell, Almkvist and Sandman,[15] Slatineano and Danielopol[16] and others, give positive reactions in a large proportion of cases, especially in the tubercular form of the disease. One of the non-syphilitic cases presenting aphthous ulcers and giving a history of their recurrence for many years, showed a moderately positive reaction with the Noguchi test, though a negative reaction with the Wassermann test. No history whatever or signs of syphilis

could be ascertained. A second examination was unfortunately not made. Finally in a single case of eczema in a young unmarried Jewess of nineteen, a negative Wassermann reaction was obtained, while the Noguchi method gave a most marked positive reaction. In this case the serum was tested by Dr. Noguchi himself. It seemed possible to rule out a previous syphilitic infection as far as this can indeed ever be done. To the great regret of the writer it has not been as yet possible to obtain a second specimen of blood for examination. As a result of finding a positive reaction in the writer's case of eczema, Noguchi personally examined with his test the sera of thirty other cases of eczema and obtained uniformly negative results in all.

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## Conclusions:

First.—Of the different methods of serum diagnosis of syphilis, depending upon the principle of complement-fixation, that of Noguchi seems most perfect from a theoretical standpoint.

Second.—From the standpoint of simplicity in technique, the method of Noguchi stands without a rival.

Third.—The result of the writer's comparative analysis of the Wassermann and Noguchi tests, shows in cases of syphilis, a larger proportion of positive reactions with the Noguchi than with the Wassermann test. It is only fair, however, to say that at present the two methods give fairly parallel results in the writer's hands.

Fourth.—Whether the Noguchi test will prove to be as nearly specific for syphilis as the original Wassermann method, can only be ascertained after an examination in the future of a large number of cases.

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